



# Comparison of pulse sequences for $R_1$ -based electron paramagnetic resonance oxygen imaging



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## ABSTRACT

Electron paramagnetic resonance (EPR) spin–lattice relaxation (SLR) oxygen imaging has proven to be an indispensable tool for assessing oxygen partial pressure in live animals. EPR oxygen images show remarkable oxygen accuracy when combined with high precision and spatial resolution. Developing more effective means for obtaining SLR rates is of great practical, biological and medical importance. In this work we compared different pulse EPR imaging protocols and pulse sequences to establish advantages and areas of applicability for each method. Tests were performed using phantoms containing spin probes with oxygen concentrations relevant to *in vivo* oxymetry. We have found that for small animal size objects the inversion recovery sequence combined with the filtered backprojection reconstruction method delivers the best accuracy and precision. For large animals, in which large radio frequency energy deposition might be critical, free induction decay and three pulse stimulated echo sequences might find better practical usage.

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## 1. Introduction

Imaging oxygen in the tissues of living animals and eventually in humans has profound health related consequence. Of the causes of human death worldwide, the four leading causes result from local tissue oxygen starvation. In first world countries seven of the leading causes are from local tissue oxygen starvation [1]. The value of oxygen images increases as their ability to absolutely quantify the average local  $pO_2$  in image voxels increases. More accurate  $pO_2$  quantification allows repeated images to be obtained with more highly resolved  $pO_2$  changes in local tissue [2]. EPR oxygen measurements and images have until recently relied on the increase in transverse relaxation rates ( $R_2 = 1/T_2$ , where  $T_2$  is the relaxation time) through Heisenberg spin exchange [3–6]. Since our very early *in vivo* oxygen image [7], a number of groups have published important contributions using EPR imaging including pulse imaging [8–11]. Recently we demonstrated that spin–lattice relaxation (SLR or  $R_1$ ) based electron paramagnetic resonance (EPR) oxygen images that use soluble spin probes are superior to

their phase relaxation based analogs [12]. Spin probe relaxation rates are linearly related to the oxygen tension of molecular oxygen when dissolved in the same solution. This facilitates high precision measurements and imaging of the oxygen tension in live animal tissues [13]. Although the SLR rates of typical spin probes are similar to phase relaxation rates, they carry much less dependence on other factors such as salinity and, especially, spin probe concentration self-relaxation or broadening. This property of SLR imaging makes it possible to obtain nearly absolute oxygen images, greatly advancing the field of *in vivo* oxymetry.

A number of approaches to oxygen imaging are possible. The development of trityl spin probes with multi-microsecond relaxation times has enabled *in vivo* EPR oxygen images using pulse techniques, pioneered by the Biophysical Spectroscopy group at the National Cancer Institute [10,14] and further pursued in our laboratory [11,15]. More traditional spectral spatial images [16,17] will not be discussed here. In this paper we examine different  $R_1$  imaging methods.

## 2. Pulse sequences and imaging methods

At present, the two major methodologies for pulse EPR *in vivo* imaging are: electron spin echo (ESE) imaging and single point imaging (SPI). Both account for the instrumental limitations imposed by microsecond-long spin probe electron relaxation

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